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FILE 'HCAPLUS' ENTERED AT 14:11:54 ON 28 SEP 2004
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FILE COVERS 1907 - 28 Sep 2004  VOL 141 ISS 14
FILE LAST UPDATED: 27 Sep 2004  (20040927/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


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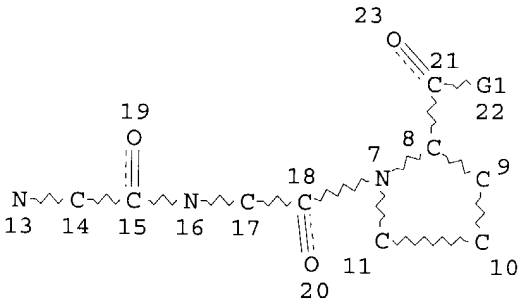


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DEFAULT ECLEVEL IS LIMITED

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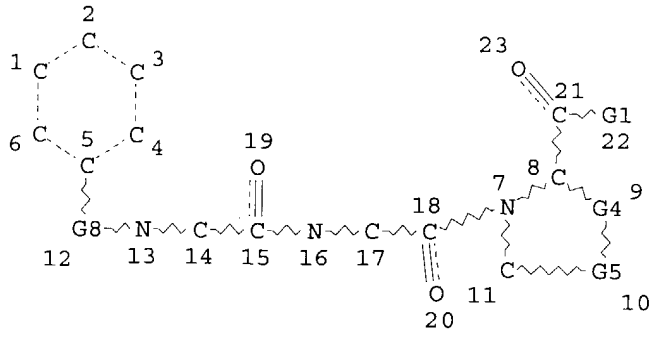

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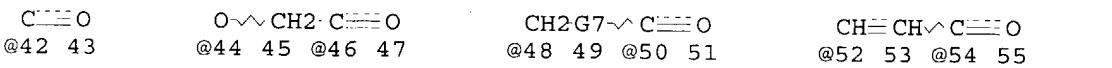

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VAR G8=42/44-5 46-13/48-5 50-13/52-5 54-13/54-5 52-13/50-5 48-13/46-5 44-
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  55

STEREO ATTRIBUTES: NONE
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=> d ibib abs hitstr l18 1-10

L18  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:353133  HCAPLUS
DOCUMENT NUMBER:          140:357670
TITLE:                    Preparation of amino acid derivatives for modulating
                          angiotensin converting enzyme-2 (ACE-2)
INVENTOR(S):              Acton, Susan L.; Ocain, Timothy D.; Gould, Alexandra
                          E.; Dales, Natalie A.; Guan, Bing; Brown, James A.;
                          Patane, Michael; Kadambi, Vivek J.; Solomon, Michael;
```

PATENT ASSIGNEE(S):	Stricker-Krongrad, Alain USA
SOURCE:	U.S. Pat. Appl. Publ., 358 pp., Cont.-in-part of U.S. Ser. No. 870,382. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004082496	A1	20040429	US 2001-999781		20011031
ZA 2001009378	A	20021114	ZA 2001-9378		20011114
PRIORITY APPLN. INFO.:			US 1999-132034P	P	19990430
			US 1999-171052P	P	19991216
			US 2000-704216	B2	20001101
			US 2001-870382	A2	20010529
			US 2001-371741P	P	20011019

OTHER SOURCE(S): MARPAT 140:357670

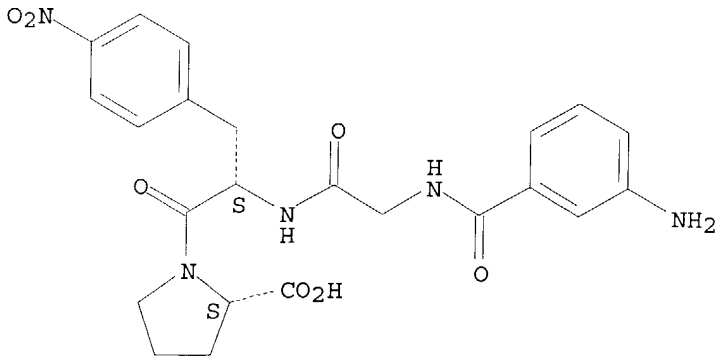
AB ACE-2 modulating compds. Z-A-B-E (Z is a zinc coordinating moiety; E is an enzyme coordinating moiety; A is an auxiliary pocket binding moiety; B is a side chain binding moiety) were prepared for the treatment of body weight disorders. Thus, N-[(S)- or (R)-1-carboxy-3-phenylpropyl]-L-leucine was prepared by the solid-phase method and showed ACE-2 inhibitory activity.

IT **305336-84-9**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(preparation of amino acid derivs. for modulating angiotensin converting enzyme-2 (ACE-2))

RN 305336-84-9 HCAPLUS

CN L-Proline, N-(3-aminobenzoyl)glycyl-4-nitro-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L18 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2002:609522 HCAPLUS
DOCUMENT NUMBER:	137:163818
TITLE:	Tripeptide derivatives for the treatment of post-**lesional** diseases of the nervous system
INVENTOR(S):	Rapin, Jean; Witzmann, Hans Klaus; Grumel, Jean-Marie; Gonella, Jacques
PATENT ASSIGNEE(S):	Tell-Pharm AG, Switz.
SOURCE:	Ger. Offen., 4 pp. CODEN: GWXXBX
DOCUMENT TYPE:	Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10105040	A1	20020814	DE 2001-10105040	20010205
WO 2002062372	A2	20020815	WO 2002-EP1182	20020205
WO 2002062372	A3	20040108		

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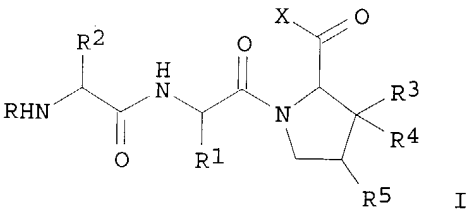
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1390055	A2	20040225	EP 2002-704686	20020205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004526701	T2	20040902	JP 2002-562378	20020205

PRIORITY APPLN. INFO.:	DE 2001-10105040	A	20010205
	WO 2002-EP1182	W	20020205

OTHER SOURCE(S): MARPAT 137:163818
GI



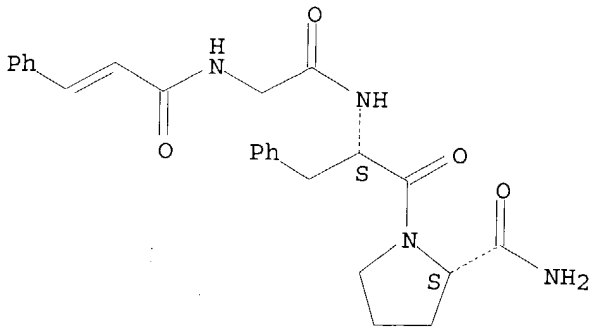
I

AB The invention discloses the use of cinnamoyl tripeptide derivs. for the treatment of post-**lesional neuronal** diseases. The cinnamoyl tripeptide derivs. are I [X = OH, C1-5 alkoxy, NH2, NH(C1-5 alkyl), N(C1-5 alkyl)2; R = (preferably) cinnamoyl; R1 = group derived from Phe, Tyr, Trp, Pro, Ala, Val, Leu or Ile; R2 = group derived from Gly, Ala, Ile, Val, Ser, Thr, His, Arg, Lys, Pro, Glu, Gln, pGlu, Asp and Asn; R3, R4 = H, OH, C1-5 alkyl, C1-5 alkoxy, provided that R3 and R4 are not both OH or C1-5 alkoxy; R5 = H, OH, C1-5 alkyl, C1-5 alkoxy], or a pharmaceutical acceptable salt thereof.

IT **123910-57-6**
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tripeptide derivs. for treatment of post-**lesional** nervous system diseases)

RN 123910-57-6 HCAPLUS
CN L-Prolinamide, N-(1-oxo-3-phenyl-2-propenyl)glycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



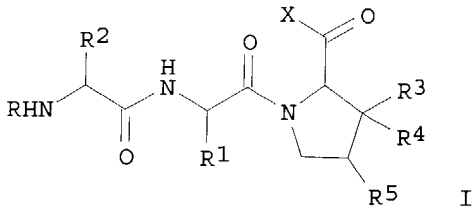
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:591566 HCAPLUS
DOCUMENT NUMBER: 137:135103
TITLE: Tripeptide derivatives for treatment of **neurodegenerative** diseases
INVENTOR(S): Rapin, Jean; Witzmann, Hans Klaus; Grumel, Jean-Marie; Gonella, Jacques
PATENT ASSIGNEE(S): Tell-Pharm A.-G., Switz.
SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10105039	A1	20020808	DE 2001-10105039	20010205
WO 2002062830	A1	20020815	WO 2002-EP1181	20020205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1358204	A1	20031105	EP 2002-716727	20020205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: DE 2001-10105039 A 20010205
WO 2002-EP1181 W 20020205

OTHER SOURCE(S): MARPAT 137:135103
GI



I

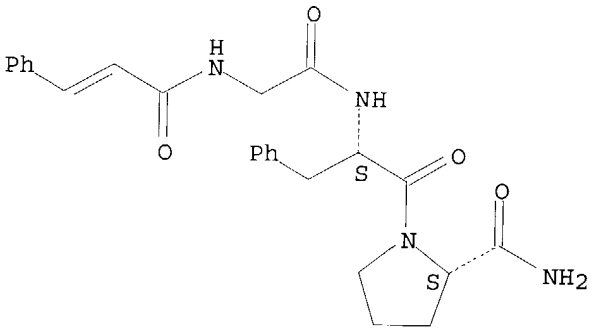
AB The invention discloses the use of tripeptide derivs. for treatment of **neurodegenerative** diseases. The tripeptide derivs. are I [X = OH, C1-5 alkoxy, NH2, NH(C1-5 alkyl), N(C1-5 alkyl)2; R = (preferably) cinnamoyl; R1 = group derived from Phe, Tyr, Trp, Pro, Ala, Val, Leu or Ile; R2 = group derived from Gly, Ala, Ile, Val, Ser, Thr, His, Arg, Lys, Pro, Glu, Gln, pGlu, Asp or Asn; R3, R4 = H, OH, C1-5 alkyl, C1-5 alkoxy, provided that R3 and R4 are not both OH or C1-5 alkoxy; R5 = H, OH, C1-5 alkyl, C1-5 alkoxy], or a pharmaceutically compatible salt. Cinnamoyl-Gly-L-Phe-L-Pro-NH2 was tested in an **Alzheimer**'s disease model.

IT **123910-57-6**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tripeptide derivs. for treatment of **neurodegenerative** diseases)

RN 123910-57-6 HCAPLUS

CN L-Prolinamide, N-(1-oxo-3-phenyl-2-propenyl)glycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L18 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:391512 HCAPLUS
DOCUMENT NUMBER: 136:402027
TITLE: Preparation of amino acid derivatives for modulating angiotensin converting enzyme-2 (ACE-2)
INVENTOR(S): Acton, Susan L.; Ocain, Timothy D.; Gould, Alexandra E.; Dales, Natalie A.; Guan, Bing; Brown, James A.; Patane, Michael; Kadambi, Vivek J.; Solomon, Michael; Stricker-Krongrad, Alain
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 395 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002039997	A2	20020523	WO 2001-US45703	20011031
WO 2002039997	A3	20021128		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002039454	A5	20020527	AU 2002-39454	20011031
PRIORITY APPLN. INFO.:			US 2000-704216 A	20001101
			US 2001-870382 A	20010529
			US 2001-371741P P	20011019
			WO 2001-US45703 W	20011031

OTHER SOURCE(S): MARPAT 136:402027

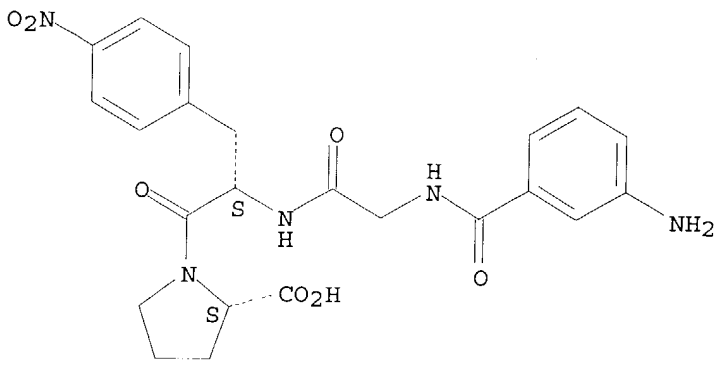
AB ACE-2 modulating compds. Z-A-B-E (Z is a zinc coordinating moiety; E is an enzyme coordinating moiety; A is an auxiliary pocket binding moiety; B is a side chain binding moiety) were prepared for the treatment of body weight disorders. Thus, N-[(S)- or (R)-1-carboxy-3-phenylpropyl]-L-leucine was prepared by the solid-phase method and showed ACE-2 inhibitory activity.

IT **305336-84-9**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(preparation of amino acid derivs. for modulating angiotensin converting enzyme-2 (ACE-2))

RN 305336-84-9 HCAPLUS

CN L-Proline, N-(3-aminobenzoyl)glycyl-4-nitro-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



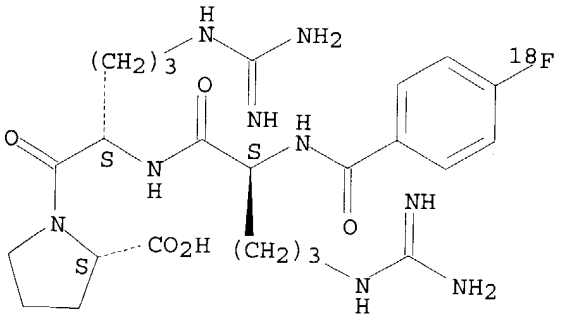
L18 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:23216 HCAPLUS
DOCUMENT NUMBER: 136:275463
TITLE: Biodistribution and catabolism of 18F-labeled **neurotensin**(8-13) analogs
AUTHOR(S): Bergmann, Ralf; Scheunemann, Matthias; Heichert, Christoph; Mading, Peter; Wittrisch, Holm; Kretzschmar, Marion; Rodig, Heike; Tourwe, Dirk;

Iterbeke, Koen; Chavatte, Kris; Zips, Daniel; Reubi, Jean Claude; Johannsen, Bernd
CORPORATE SOURCE: Institut fuer Bioanorganische und Radiopharmazeutische Chemie, Forschungszentrum Rossendorf, Germany
SOURCE: Nuclear Medicine and Biology (2002), 29(1), 61-72
CODEN: NMBIEO; ISSN: 0969-8051
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 4-([18F]fluoro)benzoyl-**neurotensin**(8-13) (18FB-Arg8-Arg9-Pro10-Tyr11- Ile12-Leu13-OH, 1) and two analogs stabilized in one and two positions (18FB-Arg8ψ(CH2NH)Arg9-Pro10-Tyr11- Ile12-Leu13-OH, 2, 18FB-Arg8ψ(CH2NH)Arg9-Pro10-Tyr11-Tle12-Leu13-OH, 3) were synthesized in a radiochem. yield of 25-36% and a specific activity of 5-15 GBq/mmol. The peptides were evaluated in vitro and in vivo for their potential to image tumors overexpressing **neurotensin** receptor 1 (NTR1) by positron emission tomog. (PET). All analogs exhibited in vitro binding affinity in the low nanomolar range to NTR1-expressing human tumors, measured by quant. receptor autoradiog., HT-29 and WiDr cells, and to sections of tumors derived from these cell lines in mice. The radiotracers were internalized in the cells in vitro, and the fluorinated peptides were able to mobilize intracellular Ca2+ of WiDr cells. In in vivo studies in rats and in mice bearing HT-29 cell tumors, only a moderate uptake of the radioligands into the studied tumors was observed, presumingly due to degradation in vivo and fast elimination by the kidneys. In comparison with the other analogs, the specific tumor uptake expressed as tumor-to-muscle relation was highest for the radioligand 3. The blood clearance of 3 was reduced by co-injection of peptidase inhibitors. The catabolic pathways of the radiofluorinated peptides were elucidated. The results suggest that the high binding affinity to NTR1 and the stabilization against proteolytic degradation are not yet sufficient for tumor imaging by PET.

IT **406486-51-9**
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(metabolite; biodistribution and catabolism of 18F-labeled **neurotensin**(8-13) analogs in relation to their potential to image tumors overexpressing **neurotensin** receptor 1 by PET)

RN 406486-51-9 HCAPLUS
CN L-Proline, N2-[4-(fluoro-18F)benzoyl]-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:338068 HCAPLUS
DOCUMENT NUMBER: 134:348237

TITLE: Treatment of female sexual arousal dysfunction
INVENTOR(S): Maw, Graham Nigel; Wayman, Christopher Peter
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: Eur. Pat. Appl., 135 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1097707	A1	20010509	EP 2000-309719	20001103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
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ZA 2000006378	A	20020506	ZA 2000-6378	20001106
NO 2000005618	A	20010509	NO 2000-5618	20001107
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NO 2000005662	A	20010509	NO 2000-5662	20001107
CN 1320426	A	20011107	CN 2000-137665	20001107
CN 1322526	A	20011121	CN 2000-137671	20001107
CN 1328824	A	20020102	CN 2000-137670	20001107
NZ 508006	A	20020628	NZ 2000-508006	20001107
NZ 508007	A	20020628	NZ 2000-508007	20001107
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BR 2000005266	A	20030408	BR 2000-5266	20001107
JP 2001206855	A2	20010731	JP 2000-339905	20001108
JP 2001213802	A2	20010807	JP 2000-339853	20001108
JP 2001247478	A2	20010911	JP 2000-339949	20001108
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BR 2000005276	A	20030408	BR 2000-5276	20001108
BR 2000005299	A	20030415	BR 2000-5299	20001108
US 6734186	B1	20040511	US 2000-708392	20001108

PRIORITY APPLN. INFO.:

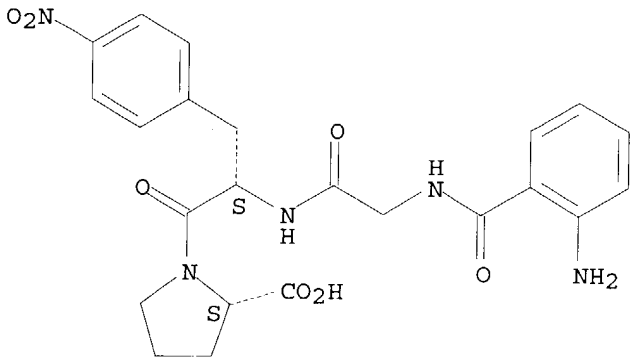
GB 1999-26437	A	19991108
GB 2000-4021	A	20000218
GB 2000-13001	A	20000526
GB 2000-16563	A	20000705
GB 2000-17141	A	20000712
US 2000-175161P	P	20000107
US 2000-192962P	P	20000329
US 2000-217479P	P	20000711
US 2000-221014P	P	20000727
US 2000-221093P	P	20000727

AB A method of treating a female suffering from female sexual dysfunction (FSD), in particular female sexual arousal dysfunction (FSAD), is described. The method comprises delivering to the female an agent that is capable of potentiating cAMP in the sexual genitalia; wherein the agent is in an amount to cause potentiation of cAMP in the sexual genitalia of the female. The agent may be admixed with a pharmaceutically acceptable carrier, diluent or excipient.

IT **67482-93-3**
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(treatment of female sexual arousal dysfunction)

RN 67482-93-3 HCAPLUS
CN L-Proline, N-(2-aminobenzoyl)glycyl-4-nitro-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:790293 HCAPLUS
DOCUMENT NUMBER: 133:344615
TITLE: ACE-2 inhibiting compounds, their preparation, pharmaceutical compositions containing them, and their therapeutic use
INVENTOR(S): Acton, Susan L.; Ocain, Timothy D.; Gould, Alexandra E.; Dales, Natalie A.; Guan, Bing; Brown, James A.
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066104	A2	20001109	WO 2000-US11550	20000428
WO 2000066104	A3	20010628		
WO 2000066104	C2	20020829		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1183019	A2	20020306	EP 2000-926478	20000428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200103094	T2	20020321	TR 2001-200103094	20000428
BR 2000010166	A	20020604	BR 2000-10166	20000428
JP 2002543120	T2	20021217	JP 2000-614989	20000428
US 6632830	B1	20031014	US 2000-561759	20000428
NO 2001005274	A	20011228	NO 2001-5274	20011029
ZA 2001009378	A	20021114	ZA 2001-9378	20011114
PRIORITY APPLN. INFO.:			US 1999-132034P P	19990430
			US 1999-171052P P	19991216

WO 2000-US11550 W 20000428

OTHER SOURCE(S): MARPAT 133:344615

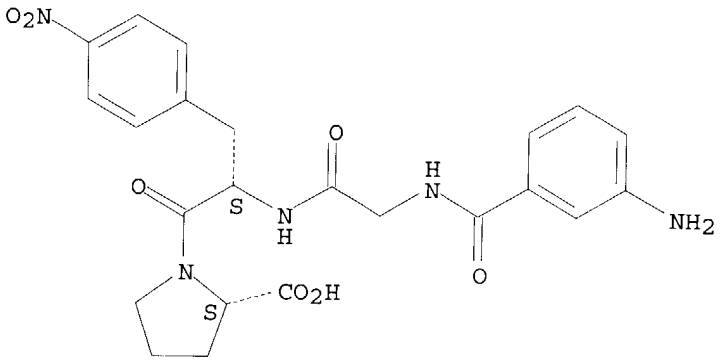
AB ACE-2 inhibiting compds. are disclosed. Methods of using the compds. and pharmaceutical compns. containing the compds. are also claimed. The compds. of the invention are useful for treating e.g. blood pressure-related diseases. Compound preparation is described.

IT **305336-84-9**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ACE-2 inhibitor preparation, pharmaceutical compns., and therapeutic use)

RN 305336-84-9 HCAPLUS

CN L-Proline, N-(3-aminobenzoyl)glycyl-4-nitro-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L18 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:124017 HCAPLUS

DOCUMENT NUMBER: 130:322240

TITLE: N-domain selectivity of angiotensin I-converting enzyme as assessed by structure-function studies of its highly selective substrate, N-acetyl-seryl-aspartyl-lysyl-proline

AUTHOR(S): Michaud, Annie; Chauvet, Marie-Therese; Corvol, Pierre

CORPORATE SOURCE: Institut National de la Sante et de la Recherche Medicale, Unite 36, College de France, Paris, 75005, Fr.

SOURCE: Biochemical Pharmacology (1999), 57(6), 611-618
CODEN: BCPCA6; ISSN: 0006-2952

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

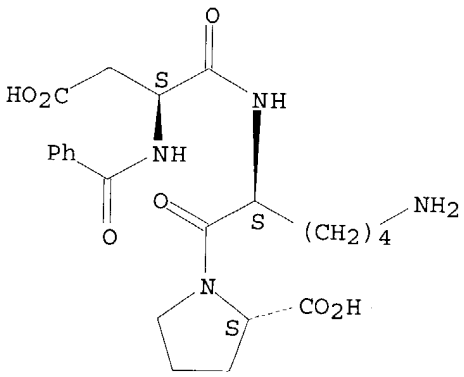
LANGUAGE: English

AB The physiol. functions of angiotensin I-converting enzyme (ACE) are not limited to its cardiovascular role. ACE constantly degrades N-acetyl-seryl-aspartyl-lysyl-proline (AcSDKP), a natural circulating regulator of the hematopoietic stem cell proliferation, and thereby may be involved in hematopoietic stem cell regulation. AcSDKP is hydrolyzed 50-fold faster by the N-domain active site compared to the C-domain active site. The aim of the present study was to investigate which amino acid residues from AcSDKP are required to ensure N-domain specificity. Several peptides were designed by progressively increasing the length of the peptidic chain from a tripeptide to a pentapeptide. Kinetic studies of the wild-type ACE and of the two ACE mutants containing a single active domain (N- or C-domain) were performed using Bz (benzoyl) Asp-Lys-Pro, benzoyl-glycyl (Bz-Gly)-Asp-Lys-Pro, and Bz-Gly-Ser-Asp-Lys-Pro (with its intermediate product Bz-Gly-Ser-Asp) as substrates. The unexpected

importance of an aspartic acid in the P1 position was discovered, as well as the interaction of the P2 and P3 positions in the substrate to increase or decrease N-domain specificity. Substrates longer than five residues may involve interdependence between subsites. Finally, the discovery of highly specific and novel N-domain substrates cannot be predicted from single subsite mapping, but may require other approaches such as combinatorial peptide libraries.

IT **223779-90-6**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(N-domain selectivity of angiotensin I-converting enzyme as assessed by structure-function studies of its highly selective substrate, N-acetyl-seryl-aspartyl-lysyl-proline)
RN 223779-90-6 HCAPLUS
CN L-Proline, N-benzoyl-L-α-aspartyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:16254 HCAPLUS
DOCUMENT NUMBER: 112:16254
TITLE: Targeted delivery of drugs and diagnostic agents using carriers which promote endothelial and epithelial uptake and **lesional** localization
INVENTOR(S): Ranney, David F.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8807365	A2	19881006	WO 1988-US1096	19880330
WO 8807365	A3	19881117		
W: AT, AU, BB, BG, BR, CH, DE, DK, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, RO, SD, SE, SU, US				
RW: AT, BE, BJ, CF, CG, CH, CM, DE, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG				
US 4925678	A	19900515	US 1987-33432	19870401
AU 8816275	A1	19881102	AU 1988-16275	19880330
AU 607494	B2	19910307		

EP 352295	A1	19900131	EP 1988-903702	19880330
EP 352295	B1	19930616		
EP 352295	B2	19960410		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 04504404	T2	19920806	JP 1988-503579	19880330
JP 2886171	B2	19990426		
AT 90554	E	19930715	AT 1988-903702	19880330
CA 1324080	A1	19931109	CA 1988-565119	19880426
US 5108759	A	19920428	US 1989-448121	19891208
PRIORITY APPLN. INFO.:			US 1987-33432	19870401
			EP 1988-903702	19880330
			WO 1988-US1096	19880330

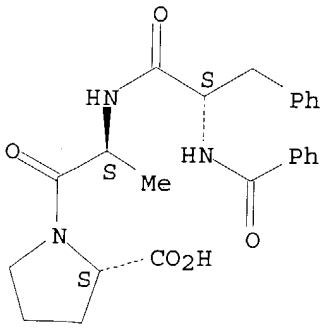
AB Targeted delivery systems comprise drugs or diagnostic agents and carriers which recognize determinants present on normal or diseased endothelium. This induces the following effects in vivo: (1) rapid endothelial envelopment of the carrier; (2) sequestration of the carrier and protection of the entrapped agent from early blood clearance; (3) acceleration of the carrier's transport across the vascular endothelium into the interstitium; and (4) improvement of drug delivery across the endothelium, so that a lower total drug dose is required. Aqueous cisplatin (I) was mixed with heparin at a 1:1.1 weight ratio and ultrasonicated to form a heparin-coated I microemulsion with particle sizes of 0.2-1.5 μm, which was stable for >1 h at 22°. Mice receiving this emulsion i.v. showed moderate to intense concentration of I in the lung interstitia, alveolar pneumocytes, respiratory epithelia, and lymph nodes, but low I concns. in the liver, whereas mice receiving standard aqueous I showed intense I concentration in the liver and almost no I in the lungs. Thus high concns. of I (which are usually toxic to endothelium) can be successfully reformulated as a heparin microemulsion, and the heparin component can induce endothelial binding and transcellular uptake of the complexes in a fashion that protects the endothelium from the toxic effects of the drug.

IT **69677-91-4**
RL: BIOL (Biological study)
(as multivalent binding agent, for targeted drug delivery to epithelium)

RN 69677-91-4 HCAPLUS

CN L-Proline, N-benzoyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L18 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1989:633680 HCAPLUS
DOCUMENT NUMBER:	111:233680
TITLE:	Preparation of tripeptides containing L-proline derivatives as nootropics and pharmaceutical compositions containing them
INVENTOR(S):	Fiez-Vandal, Pierre Yves

PATENT ASSIGNEE(S): Inorgan S. A., Switz.
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 316218	A1	19890517	EP 1988-402761	19881103
EP 316218	B1	19930915		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2622581	A1	19890505	FR 1987-15228	19871103
FR 2622581	B1	19900216		
JP 01157998	A2	19890621	JP 1988-276343	19881102
FI 8805083	A	19890504	FI 1988-5083	19881103
US 5212158	A	19930518	US 1988-266680	19881103
AT 94560	E	19931015	AT 1988-402761	19881103
ES 2061710	T3	19941216	ES 1988-402761	19881103
KR 121793	B1	19971127	KR 1988-14433	19881103
CA 1340227	A1	19981215	CA 1988-582169	19881103

PRIORITY APPLN. INFO.: FR 1987-15228 A 19871103
EP 1988-402761 A 19881103

OTHER SOURCE(S): CASREACT 111:233680; MARPAT 111:233680
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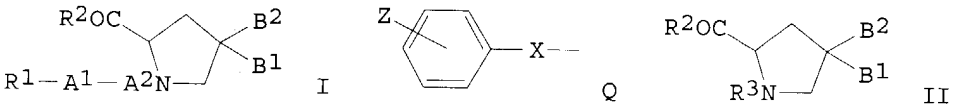


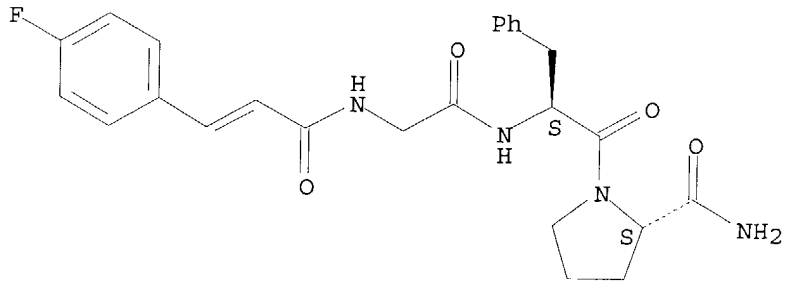
AB The title compds. [I; R1 = Q; X = CO, YCO, OYCO; Y = alkylene, alkenylene; Z = H, ≥1 CF3, alkyl, alkylenedioxy; R2 = NH2, OH, or a functional derivative thereof; A1, A2 = amino acid residue; B1, B2 = H, Me] and their pharmaceutically acceptable salts, useful as nootropics for treatment of **senile** dementia, **Alzheimer**'s disease, Parkinson's disease, schizophrenia, and depression, are prepared via reaction of activated R1-A1-OH with proline derivs. II (R3 = H-A2), obtained by reaction of II (R3 = H) with activated H-A2-OH. N-Cinnamoylglycine (preparation given) was condensed with II.CF3CO2H (R2 = NH2, B1 = B2 = H, R3 = H-Phe)(preparation given) in DMF containing dicyclohexylcarbodiimide and N-methylmorpholine to give I (R1 = cinnamoyl, R2 = NH2, B1 = B2 = H, A1 = Gly, A2 = Phe) (III). III, administered i.p. or p.o. at 1 mg/kg, was effective in antagonizing scopolamine-induced amnesia in mice.

IT **123910-50-9P 123910-52-1P 123910-53-2P**
123910-54-3P 123910-55-4P 123910-57-6P
123910-58-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as nootropic)

RN 123910-50-9 HCAPLUS

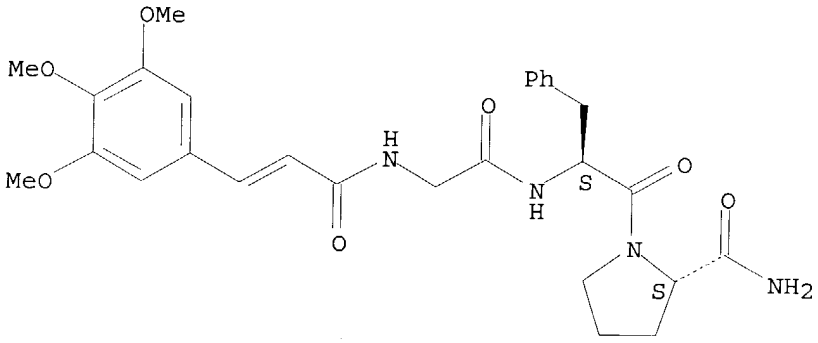
CN L-Prolinamide, N-[3-(4-fluorophenyl)-1-oxo-2-propenyl]glycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



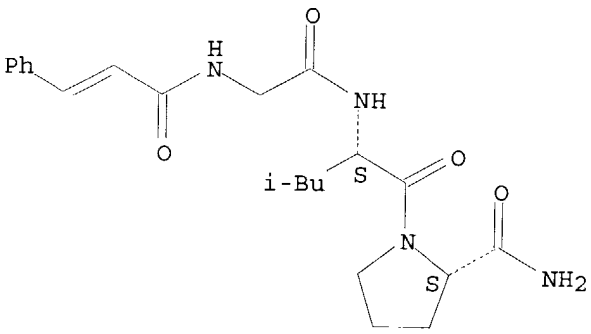
RN 123910-52-1 HCAPLUS
CN L-Prolinamide, N-[1-oxo-3-(3,4,5-trimethoxyphenyl)-2-propenyl]glycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



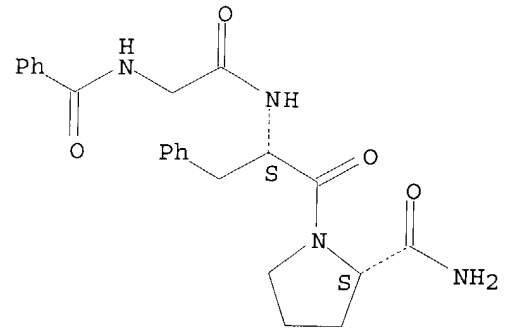
RN 123910-53-2 HCAPLUS
CN L-Prolinamide, N-(1-oxo-3-phenyl-2-propenyl)glycyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



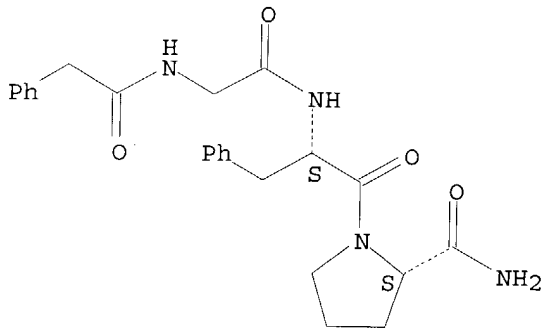
RN 123910-54-3 HCAPLUS
CN L-Prolinamide, N-benzoylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



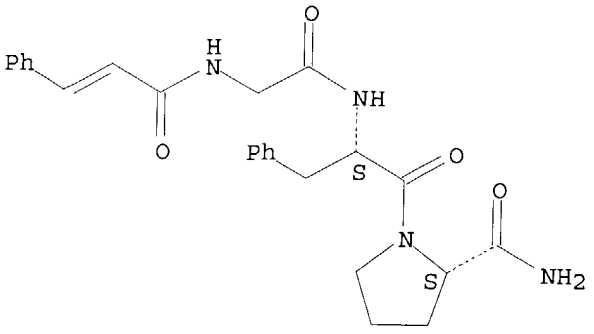
RN 123910-55-4 HCAPLUS
CN L-Prolinamide, N-(phenylacetyl)glycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



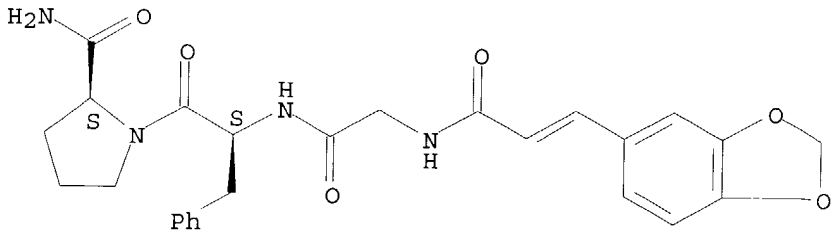
RN 123910-57-6 HCAPLUS
CN L-Prolinamide, N-(1-oxo-3-phenyl-2-propenyl)glycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 123910-58-7 HCAPLUS
CN L-Prolinamide, N-[3-(1,3-benzodioxol-5-yl)-1-oxo-2-propenyl]glycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



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L29 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:354079 HCAPLUS
DOCUMENT NUMBER: 136:355487
TITLE: Preparation of meta-benzamidine derivatives of amino acids or dipeptides as serine protease inhibitors
INVENTOR(S): Liebeschuetz, John Walter; Wylie, William Alexander; Waszkowycz, Bohdan; Murray, Christopher William; Rimmer, Andrew David; Welsh, Pauline Mary; Jones, Stuart Donald; Roscoe, Jonathan Michael Ernest; Young, Stephen Clinton; Morgan, Phillip John
PATENT ASSIGNEE(S): Tularik Ltd., UK
SOURCE: U.S. Pat. Appl. Publ., 35 pp., Cont.-in-part of U.S. Ser. No. 485,678.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002055522	A1	20020509	US 2001-988082	20011119
US 6740682	B2	20040525		
WO 9911658	A1	19990311	WO 1998-GB2605	19980828
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2000077027	A2	20001221	WO 2000-GB2291	20000613
WO 2000077027	A3	20010525		
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US 2004143018	A1	20040722	US 2004-752568	20040108

PRIORITY APPLN. INFO.:

GB 1997-18392	A	19970829
GB 1998-3173	A	19980213
WO 1998-GB2605	W	19980828
GB 1999-13823	A	19990614
US 1999-142064P	P	19990702
US 2000-485678	A2	20000225
WO 2000-GB2291	A2	20000613
GB 1999-18741	A	19990809
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WO 2001-GB2566 W 20010612
US 2001-988082 A1 20011119

OTHER SOURCE(S): MARPAT 136:355487

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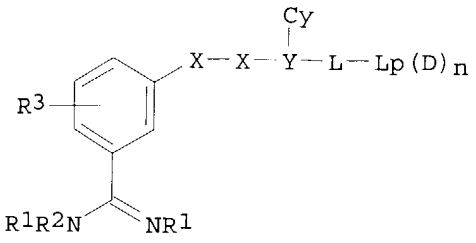


I

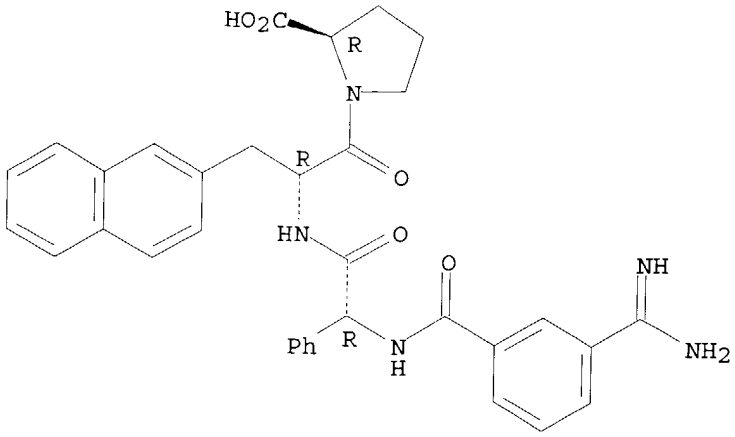
AB Title compds. I [R1, R2 = H, OH, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl, cycloalkyl; R3 = R1, R2, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulfonyl, alkylsulfenyl, alkylsulfonamido, alkylaminosulfonyl, haloalkoxy, haloalkyl; X = C, N, O, S, CO, CR1, C(R1)2, NR1 with at least one X being C, CO, CR1 or C(R1)2, with the proviso that if the benzamidine group is unsubstituted and the X-X group is -CH2C(R1)2-, then R1 = H or attached to the alkylene carbon atom by a heteroatom; L = organic linker containing 1-5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; Y = N, CR1; YL = cyclic group; Cy = (un)saturated, (poly)cyclic, (hetero)cyclic group optionally substituted by groups R3 or Ph optionally substituted by R3; Lp = lipophilic alkyl, heterocyclic, alkenyl, alkaryl, (poly)cycloalkyl, cycloalkenyl, aryl, aralkyl, haloalkyl, or a combination of two or more such groups optionally substituted by oxa, oxo, aza, thio, halo, amino, hydroxy or by R3; D = H bond donor group; n = 0-2], or corresponding compds. in which the (un)substituted amidino group R1R2NC(:NR1) is replaced with an (un)substituted aminomethyl group, or their physiol. tolerable salts were prepared as serine protease inhibitors useful as antithrombotic agents. 3-Amidino- and 3-(aminomethyl)benzoyl-D-phenylglycine 4-aminomethylcyclohexylmethylamide are among 190 compds. synthesized.

IT **221233-25-6P 221234-79-3P 221277-36-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of meta-benzamidine derivs. of amino acids or dipeptides as serine protease inhibitors)

RN 221233-25-6 HCAPLUS

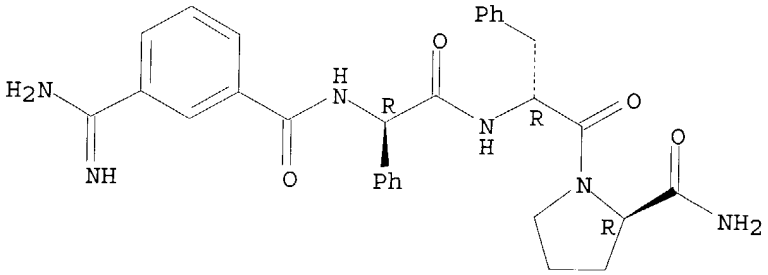
CN D-Proline, (2R)-N-[3-(aminoiminomethyl)benzoyl]-2-phenylglycyl-3-(2-naphthalenyl)-D-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



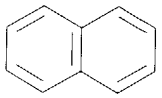
RN 221234-79-3 HCAPLUS
CN D-Prolinamide, (2R)-N-[3-(aminoiminomethyl)benzoyl]-2-phenylglycyl-D-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

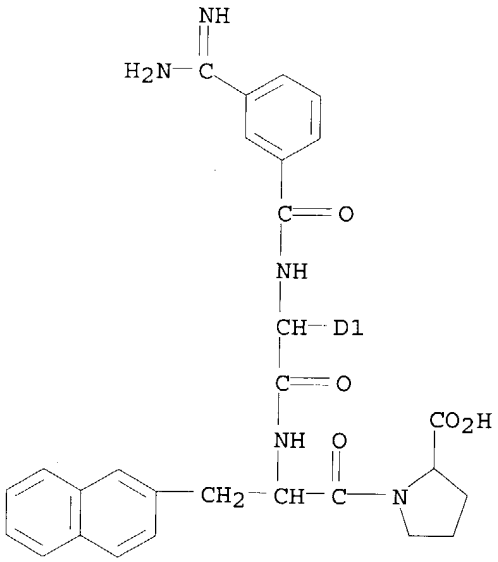


RN 221277-36-7 HCAPLUS
CN D-Proline, (2R)-N-[3-(aminoiminomethyl)benzoyl]-2-(naphthalenyl)glycyl-3-(2-naphthalenyl)-D-alanyl- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

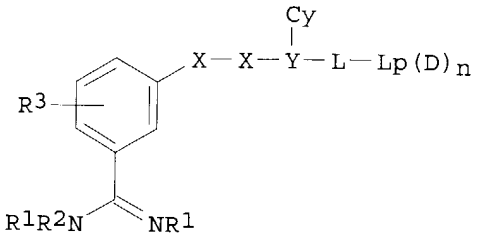


L29 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:184269 HCAPLUS
DOCUMENT NUMBER: 130:237884
TITLE: Preparation of meta-benzamidine derivatives of amino acids or dipeptides as serine protease inhibitors
INVENTOR(S): Liebeschuetz, John Walter; Wylie, William Alexander; Waszkowycz, Bohdan; Murray, Christopher William; Rimmer, Andrew David; Welsh, Pauline Mary; Jones, Stuart Donald; Roscoe, Jonathan Michael Ernest; Young, Stephen Clinton; Morgan, Phillip John
PATENT ASSIGNEE(S): Proteus Molecular Design Ltd., UK
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911658	A1	19990311	WO 1998-GB2605	19980828
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9888757	A1	19990322	AU 1998-88757	19980828
EP 1009758	A1	20000621	EP 1998-940430	19980828
R: DE, FR, GB, IT				
US 2002055522	A1	20020509	US 2001-988082	20011119
US 6740682	B2	20040525		
US 2003216403	A1	20031120	US 2003-296245	20030514
US 2004143018	A1	20040722	US 2004-752568	20040108
PRIORITY APPLN. INFO.:			GB 1997-18392 A	19970829

GB 1998-3173	A	19980213
WO 1998-GB2605	W	19980828
GB 1999-13823	A	19990614
US 1999-142064P	P	19990702
US 2000-485678	A2	20000225
WO 2000-GB2291	A2	20000613
WO 2001-GB2566	W	20010612
US 2001-988082	A1	20011119

OTHER SOURCE(S): MARPAT 130:237884
GI



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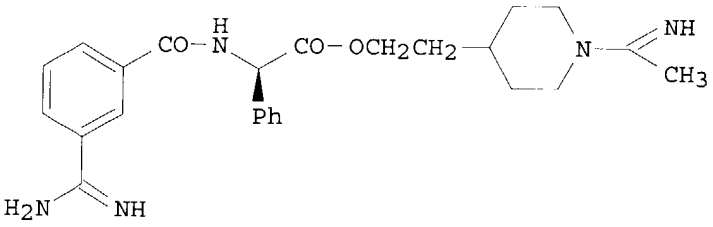


II

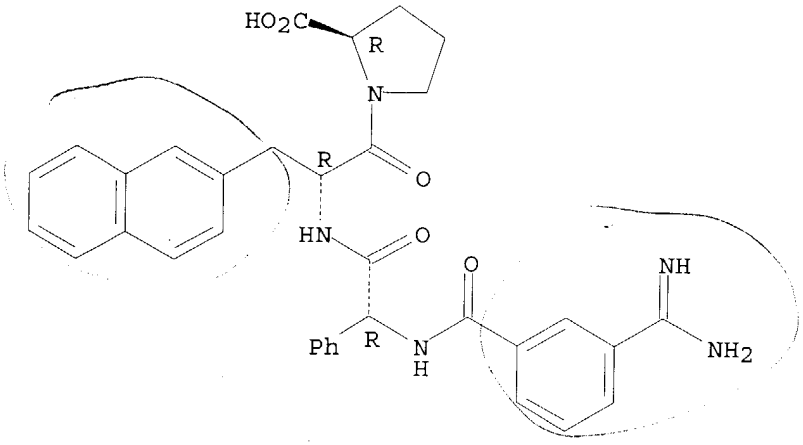
AB Title compds. I [R1, R2 = H, OH, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl, cycloalkyl; R3 = R1, R2, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulfonyl, alkylsulfenyl, alkylsulfonamido, alkylaminosulfonyl, haloalkoxy, haloalkyl; X = C, N, O, S, CO, CR1, C(R1)2, NR1 with at least one X being C, CO, CR1 or C(R1)2, with the proviso that if the benzamidine group is unsubstituted and the X-X group is -CH2C(R1)2-, then R1 = H or attached to the alkylene carbon atom by a heteroatom; L = organic linker containing 1-5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; Y = N, CR1; YL = cyclic group; Cy = (un)saturated, (poly)cyclic, (hetero)cyclic group optionally substituted by groups R3 or Ph optionally substituted by R3; Lp = lipophilic alkyl, heterocyclic, alkenyl, alkaryl, (poly)cycloalkyl, cycloalkenyl, aryl, aralkyl, haloalkyl, or a combination of two or more such groups optionally substituted by oxa, oxo, aza, thio, halo, amino, hydroxy or by R3; D = H bond donor group; n = 0-2] and their physiol. tolerable salts were prepared as serine protease inhibitors useful as antithrombotic agents. Synthesis methodol. for preparing some I was provided, and common starting materials were Fmoc- or Boc-(D)-phenylglycine and m-amidinobenzoic acid. Descriptions of enzyme assays were given, but no enzyme inhibition data was provided for I. To measure the antithrombotic activity, a partial thromboplastin time test assay was done, and for example, m-amidinobenzoyl-D-phenylglycine ester II (preparation not given, but 1H NMR characterization data provided), at 1.9 μM concentration, doubled the clotting

time.

IT **221233-25-6P 221234-79-3P 221277-36-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of meta-benzamidine derivs. of amino acids or dipeptides as serine protease inhibitors)

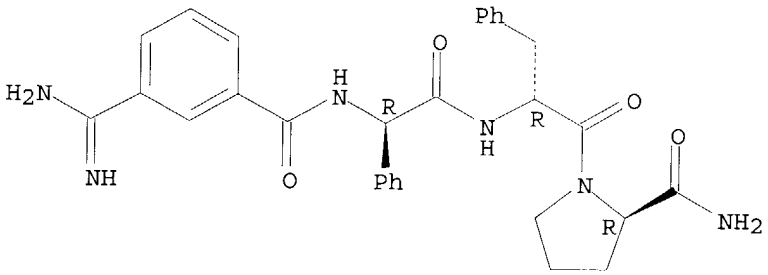
RN 221233-25-6 HCAPLUS
CN D-Proline, (2R)-N-[3-(aminoiminomethyl)benzoyl]-2-phenylglycyl-3-(2-naphthalenyl)-D-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



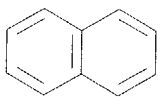
RN 221234-79-3 HCAPLUS
CN D-Prolinamide, (2R)-N-[3-(aminoiminomethyl)benzoyl]-2-phenylglycyl-D-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

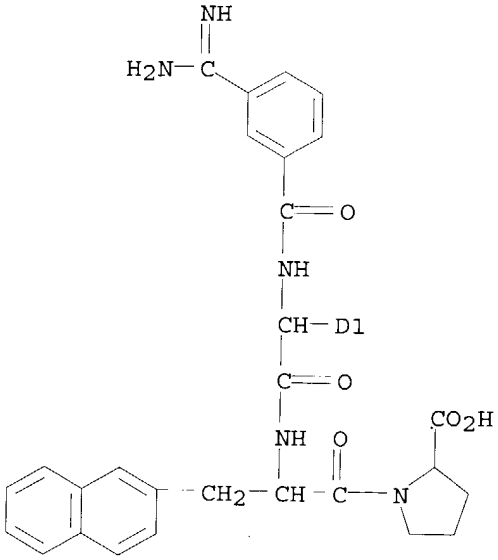


RN 221277-36-7 HCAPLUS
CN D-Proline, (2R)-N-[3-(aminoiminomethyl)benzoyl]-2-(naphthalenyl)glycyl-3-(2-naphthalenyl)-D-alanyl- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:184268 HCAPLUS
DOCUMENT NUMBER: 130:223587
TITLE: 1-amino-7-isoquinoline derivatives as serine protease inhibitors
INVENTOR(S): Liebeschuetz, John Walter; Wylie, William Alexander; Waszkowycz, Bohdan; Murray, Christopher William; Rimmer, Andrew David; Welsh, Pauline Mary; Jones, Stuart Donald; Roscoe, Jonathan Michael Ernest; Young, Stephen Clinton; Morgan, Phillip John; Camp, Nicholas Paul; Crew, Andrew Philip Austin
PATENT ASSIGNEE(S): Proteus Molecular Design Ltd., UK
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911657	A1	19990311	WO 1998-GB2600	19980828
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9888753	A1	19990322	AU 1998-88753	19980828
EP 1012166	A1	20000628	EP 1998-940425	19980828
EP 1012166	B1	20031029		
R: CH, DE, ES, FR, GB, IT, LI, NL				

US 6262069	B1	20010717	US 2000-485677		20000225
US 2002040144	A1	20020404	US 2001-865418		20010529
US 6420438	B1	20020716	US 2000-865418		20010529
US 2003216403	A1	20031120	US 2003-296245		20030514
PRIORITY APPLN. INFO.:			GB 1997-18392	A	19970829
			GB 1998-3173	A	19980213
			WO 1998-GB2600	W	19980828
			US 2000-485677	A1	20000225
			WO 2001-GB2566	W	20010612

OTHER SOURCE(S): MARPAT 130:223587
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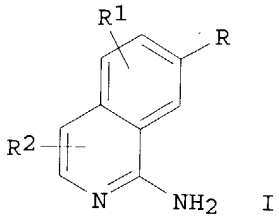


I

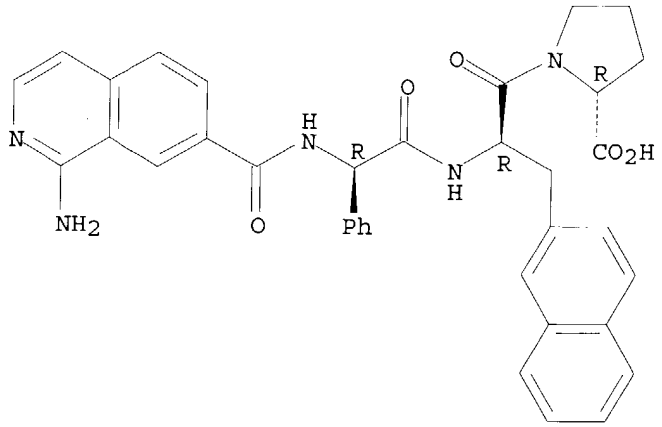
AB Aminoisoquinoline amino acid derivs. I [R1 = H, halo, cyano, nitro, hydroxy, amino, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, thiol, alkylthio, aminosulfonyl, alkoxyalkyl, alkoxycarbonyl, acyloxymethoxycarbonyl or alkylamino (optionally substituted); R2 = H, halo, Me, amino, hydroxy, or oxo; and R is X-X-Y(R7)-L-Lp(D)n, where each X independently is a C, N, O or S atom or a CO, CR1, CR12 or NR1 group; Y is a nitrogen atom or a CR1 group or Y and L taken together form a cyclic group; R7 is a lipophilic group selected from alkyl, alkenyl, mono- or bi-cycloalkyl, aryl, heteroaryl, mono- or bicycloalkylalkyl, mono- or bicycloalkylalkenyl, aralkyl, heteroaryl-alkyl, arylalkenyl, heteroarylalkenyl, all optionally substituted by a group R1; L is an organic linker group containing 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; Lp is a lipophilic organic group selected from alkyl, heterocyclic, alkenyl, alkaryl, cycloalkyl, polycycloalkyl, cycloalkenyl, aryl, aralkyl or haloalkyl group or a combination of two or more such groups optionally substituted by one or more of oxa, thia, aza or R1 groups; D is a hydrogen bond donor group; and n is 0, 1, or 2] or their 3,4-dihydro derivs. were prepared as serine protease inhibitors. Thus, 1-aminoisoquinolin-7-oyl-D-phenylglycine-4-methoxybenzylamide was prepared by amidation of Boc-D-phenylglycine with 4-methylbenzylamine, followed by deprotection and coupling with 1-aminoisoquinoline-7-carboxylic acid trifluoroacetate.

IT **221049-80-5P 221050-78-8P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoisoquinoline peptidyl derivs. as serine protease inhibitors)

RN 221049-80-5 HCAPLUS

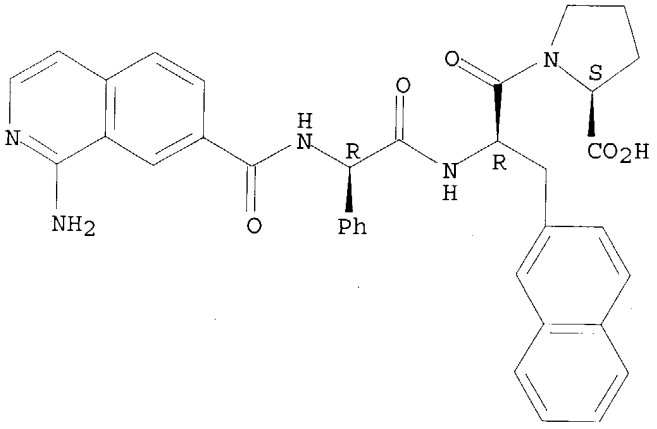
CN D-Proline, (2R)-N-[(1-amino-7-isoquinolinyl)carbonyl]-2-phenylglycyl-3-(2-naphthalenyl)-D-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 221050-78-8 HCAPLUS
CN L-Proline, (2R)-N-[(1-amino-7-isoquinolinyl)carbonyl]-2-phenylglycyl-3-(2-naphthalenyl)-D-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:581373 HCAPLUS
DOCUMENT NUMBER: 115:181373
TITLE: Bispecific monoclonal antibody to cancer cell and to enzyme with prodrug-activating characteristics, and preparation of peptidated anticancer prodrugs
INVENTOR(S): Iwasa, Susumu; Okamoto, Kayoko
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9109134	A1	19910627	WO 1990-JP1631	19901214

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE

EP 505566	A1	19920930	EP 1991-900329	19901214
JP 05506563	T2	19930930	JP 1991-501001	19901214
PRIORITY APPLN. INFO.:			JP 1989-326545	19891215
			JP 1990-97323	19900411
			JP 1990-301608	19901106
			WO 1990-JP1631	19901214

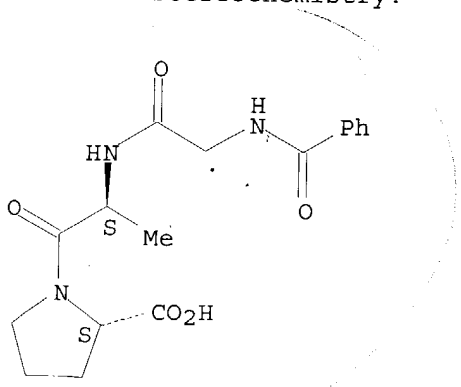
AB A hybrid bispecific monoclonal antibody (MAb) is provided having specificities against a human cancer cell and a prodrug-activating enzyme . Also provided is a polydoma producing the MAb, an antihuman cancer protein complex (the MAb-prodrug-activating enzyme complex), and methods for using the MAb in combination with an anticancer prodrug for cancer therapy. Preparation of a variety of peptidated anticancer agent prodrugs is described, as is their activity before and after proteolytic cleavage. A hybridoma producing an antihuman transferrin receptor MAb was fused with a hybridoma producing an antiurokinase MAb, and the bispecific MAb produced was purified. A complex of the bispecific MAb and urokinase was incubated with human epidermoid carcinoma cell line A431; this was followed by incubation with the prepared prodrug Boc-Gly-Gly-Arg-Val-adriamycin (Boc = t-butyloxycarbonyl). The prodrug was activated by the bispecific antibody-urokinase complex and showed strong cytotoxicity against the A431 target cells.

IT **73167-84-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in peptidated antitumor **prodrug** preparation)

RN 73167-84-7 HCAPLUS

CN L-Proline, 1-[N-(N-benzoylglycyl)-L-alanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1990:74402 HCAPLUS
DOCUMENT NUMBER:	112:74402
TITLE:	Hydrolysis of a synthetic angiotensin-converting enzyme substrate in dog lungs
AUTHOR(S):	Linehan, John H.; Bronikowski, Thomas A.; Rickaby, David A.; Dawson, Christopher A.
CORPORATE SOURCE:	Dep. Biomed. Eng., Marquette Univ., Milwaukee, WI, 53233, USA
SOURCE:	American Journal of Physiology (1989), 257(6, Pt. 2), H2006-H2016 CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The saturable kinetics of the hydrolysis of a synthetic substrate,

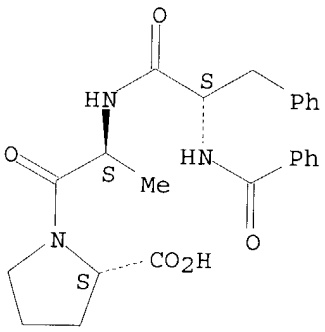
benzoyl-Phe-Ala-Pro (BPAP), for angiotensin-converting enzyme (ACE), by the pulmonary endothelium of the dog were evaluated with a multiple indicator dilution method. In the expts., isolated dog lung lobes were perfused with a salt solution containing 5% bovine serum albumin. Boluses containing [3H]BPAP, and various amts. of unlabeled BPAP were injected into the lobar artery, and timed samples of venous effluent were collected. The samples were analyzed to determine the fractional hydrolysis of the injected BPAP. The BPAP hydrolysis on passage through the lungs exhibited the saturable behavior and the relative insensitivity to changing flow rate previously described. Since it was described previously that BPAP behaves as if it exists in 2 forms, 1 of which is virtually unhydrolyzable on a single pass through the lungs, a model was formulated to include the influence of the unhydrolyzable form, as well as the saturable hydrolysis of the hydrolyzable form, on the fractional hydrolysis of the injected BPAP. This model provides a new method for estimating the kinetic parameters of BPAP hydrolysis by pulmonary endothelial ACE, and it explains the observation that the fractional BPAP hydrolysis does not vary with flow rate and transit time to the extent predicted by previous models.

IT **69677-91-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrolysis of, by angiotensin-converting enzyme of lung endothelium, kinetics of, model for)

RN 69677-91-4 HCAPLUS

CN L-Proline, N-benzoyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1989:625889 HCAPLUS

DOCUMENT NUMBER: 111:225889

TITLE: Metabolic and pharmacokinetic activity of the isolated sheep bronchial circulation

AUTHOR(S): Grantham, C. J.; Jackowski, J. T.; Wanner, A.; Ryan, U. S.

CORPORATE SOURCE: Mt. Sinai Med. Cent., Univ. Miami, Miami, FL, 33101, USA

SOURCE: Journal of Applied Physiology (1989), 67(3), 1041-7
CODEN: JAPHEV; ISSN: 8750-7587

DOCUMENT TYPE: Journal

LANGUAGE: English

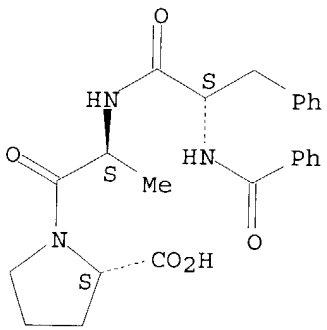
AB Bronchial vascular metabolic and pharmacokinetic activity toward benzoyl-Phe-Ala-Pro (BPAP), and ADP, adenosine, and PGE2 was studied by developing an isolated sheep bronchial circulation preparation Mean transit time (.hivin.t), uptake, and metabolism were measured by injecting [3H]-labeled substrates with [14C]sucrose into the bronchial artery of sheep lungs stripped clean of parenchymal tissue. After [3H]BPAP the .hivin.t for 3H was the same as for 14C. Thirty-six percent of the

injected BPAP was converted to metabolite ([3H]benzoyl-Phe) in a single pass. An inhibitor of angiotensin-converting enzyme, SQ 20,881, depressed BPAP metabolism by 50%, whereas perfusion of the bronchial circulation with glutaraldehyde reduced metabolism to a basal level. After [3H]ADP the .hivin.t for 3H was again the same as for 14C. 3H recovery after 40 pmol [3H]ADP was less (58%) than after 400 nmol [3H]ADP (79%). Twenty-two percent of the injected radioactivity emerged in the effluent as metabolites of ADP for either dose. Adenosine and PGE2 uptake was negligible, and most of the recovered radioactivity in each case was unchanged substrate. Evidently, the bronchial circulation is pharmacokinetically and metabolically active with respect to vasoactive mediators like angiotensin I, bradykinin, and adenine nucleotides, and the enzymes responsible for this metabolic activity line the vascular lumen.

IT **69677-91-4**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism and **pharmacokinetics** of, in bronchial circulation)

RN 69677-91-4 HCAPLUS
CN L-Proline, N-benzoyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:571581 HCAPLUS
DOCUMENT NUMBER: 111:171581
TITLE: Effect of transit time on metabolism of a pulmonary endothelial enzyme substrate
AUTHOR(S): Dawson, Christopher A.; Bongard, Robert D.; Rickaby, David A.; Linehan, John H.; Roerig, David L.
CORPORATE SOURCE: Dep. Physiol., Med. Coll. Wisconsin, Milwaukee, WI, 53226, USA
SOURCE: American Journal of Physiology (1989), 257(3, Pt. 2), H853-H865
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fractional hydrolysis (M) of the synthetic angiotensin-converting enzyme (ACE) substrate [3H]benzoyl-Phe-Ala-Pro (BPAP) on passage through the isolated dog lung lobe was relatively independent of flow rate and transit time (t). The most commonly expressed explanation for this kind of observation is that recruitment of ACE-containing surface area occurs when flow is increased. To test this, as well as other hypotheses that might explain the behavior of this substrate, M obtained after the 1st pass of a BPAP-containing bolus through isolated rabbit lungs was compared with that obtained after 2 sequential passes through the lungs. In this way, t could be doubled with no change in flow or vascular pressure. When the 2nd pass occurred within a few seconds of the first, M after both the 1st

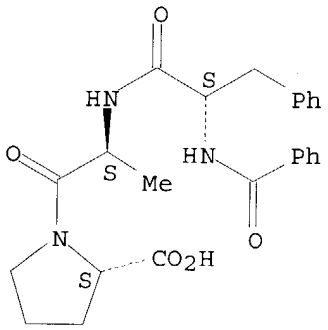
and 2nd pass was only slightly larger than that after the 1st pass alone. If the time between passes was increased to a few minutes, M after the 2nd pass was substantially increased. These results are contrary to the recruitment hypothesis and suggest that this substrate may exist in alternative forms that are in slow equilibrium relative to the capillary t. When albumin was present in the perfusate, an albumin-bound fraction appeared to be 1 such alternative form. However, expts. carried out using protein-free perfusate suggest the possibility that conformational variants of the substrate may also exist.

IT **69677-91-4**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of, by angiotensin-converting enzyme of pulmonary endothelium, transit time effect on)

RN 69677-91-4 HCAPLUS

CN L-Proline, N-benzoyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1988:523935 HCAPLUS

DOCUMENT NUMBER: 109:123935

TITLE: Pulmonary angiotensin-converting enzyme activity in the oxygen-toxic sheep

AUTHOR(S): Howell, Ralph E.; Hansen-Flaschen, John H.; Wheeldon, Eric B.

CORPORATE SOURCE: Sch. Med., Univ. Pennsylvania, Philadelphia, PA, USA

SOURCE: American Review of Respiratory Disease (1988), 138(1), 160-6
CODEN: ARDSBL; ISSN: 0003-0805

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The activity of pulmonary endothelial angiotensin-converting enzyme (ACE) was studied in 5 unanesthetized adult sheep that breathed 100% O via tracheostomy for 3 days and in 4 other sheep that breathed compressed air. In contrast to the sheep that breathed air, the sheep that breathed O developed substantial arterial hypoxemia and hypercapnia, an increased alveolar-to-arterial O gradient, and a slight respiratory acidosis. Morphol. examination of lungs from sheep that breathed O revealed a multifocal distribution of injury, including interstitial edema, capillary endothelial damage, and alveolar epithelial damage. Indicator-dilution methods were used to assess first-pass pulmonary metabolism of the ACE substrate [3H]benzoyl-Phe-Ala-Pro (BPAP) and the apparent kinetics (KM and Vmax) of ACE activity. Pulmonary metabolism of BPAP exhibited saturability, was reduced by an ACE inhibitor (enalaprit), and did not result from the activity of circulating plasma ACE. There was no difference between the 2 groups of sheep in the percent metabolism of either 0.1 μmol BPAP/kg or 1.0

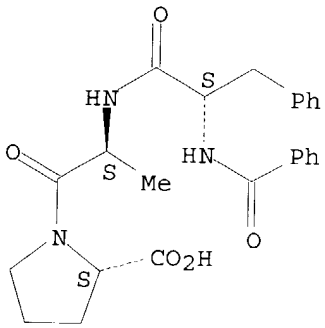
μmol BPAP/kg or in the KM of BPAP metabolism In both groups, the Vmax and Vmax/KM decreased as a result of redns. in cardiac output and volume of distribution. To further examine pulmonary endothelial ACE activity, the first-pass pulmonary uptake of an ACE inhibitor, [14C]captopril, was assessed in 4 addnl. sheep that breathed O; [14C]captopril uptake remained unchanged from control. Evidently, in sheep, 3 days of O breathing causes moderately severe gas exchange abnormalities and capillary damage without impairing pulmonary endothelial ACE activity.

IT **69677-91-4**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of, by lung, angiotensin-converting enzyme in relation to)

RN 69677-91-4 HCAPLUS

CN L-Proline, N-benzoyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1988:16827 HCAPLUS

DOCUMENT NUMBER: 108:16827

TITLE: Effect of flow and surface area on angiotensin-converting enzyme activity in rabbit lungs

AUTHOR(S): Moalli, Richard; Pitt, Bruce R.; Gillis, C. Norman

CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, 06510, USA

SOURCE: Journal of Applied Physiology (1987), 62(5), 2042-50
CODEN: JAPHEV; ISSN: 8750-7587

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Pulmonary angiotensin-converting enzyme (ACE) is located on the luminal surface of pulmonary microvasculature. Multiple indicator-dilution techniques were used to measure pulmonary ACE activity in vivo and in isolated lungs. Apparently, ACE activity is depressed in several forms of acute lung injury. Depression of ACE activity may reflect impaired substrate delivery to enzyme sites because of flow-related reduction of perfused surface area. To assess the role of altered microvascular flow and surface area in the measurement of ACE activity, similar techniques were used to estimate the apparent Km and Vmax of pulmonary ACE in isolated, Krebs-perfused rabbit lungs. Km Is an estimate of the affinity of a synthetic ACE substrate, [3H]PhCO-Phe-Ala-Pro-OH, for ACE and should not be influenced by the rate of substrate delivery to luminal enzyme sites. Conversely, Vmax is an index of the number of ACE sites and should be influenced by perfusion changes that alter the number of perfused sites (recruitment or derecruitment). When isolated lungs were subjected to physiol. maneuvers designed to increase or decrease perfused surface area, apparent Vmax increased or decreased resp. Apparent Km was not altered by these maneuvers. Km And Vmax were independent of changes in perfusion rate when surface area was held constant Thus, these parameters should be

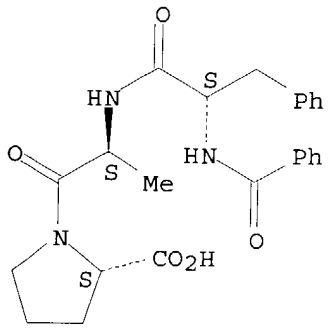
useful in evaluating perfusion changes in normal and injured lungs.

IT **69677-91-4**, Benzoyl-phenylalanyl-alanyl-proline
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with angiotensin-converting enzyme of lung, kinetics of)

RN 69677-91-4 HCAPLUS

CN L-Proline, N-benzoyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1987:618077 HCAPLUS
DOCUMENT NUMBER: 107:218077
TITLE: Preparation of LHRH analogs
INVENTOR(S): Horvath, Aniko; Keri, Gyoergy; Gulyas, Tamas; Teplan, Istvan; Vigh, Sandor; Bokonyi, Gyorgy
PATENT ASSIGNEE(S): Innofinance Altalanos Innovacios Penzintezet, Hung.
SOURCE: Ger. Offen., 15 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3700166	A1	19870709	DE 1987-3700166	19870105
HU 43090	A2	19870928	HU 1986-16	19860103
HU 194913	B	19880328		
NL 8603291	A	19870803	NL 1986-3291	19861223
JP 62228099	A2	19871006	JP 1986-309288	19861227
JP 06031314	B4	19940427		
CH 670830	A	19890714	CH 1986-5230	19861229
FI 8605347	A	19870704	FI 1986-5347	19861230
FI 85866	B	19920228		
FI 85866	C	19920610		
SE 8700016	A	19870704	SE 1987-16	19870102
GB 2185025	A1	19870708	GB 1987-17	19870102
GB 2185025	B2	19891228		
FR 2595705	A1	19870918	FR 1987-6	19870102
FR 2595705	B1	19901012		
US 4758552	A	19880719	US 1987-177	19870102

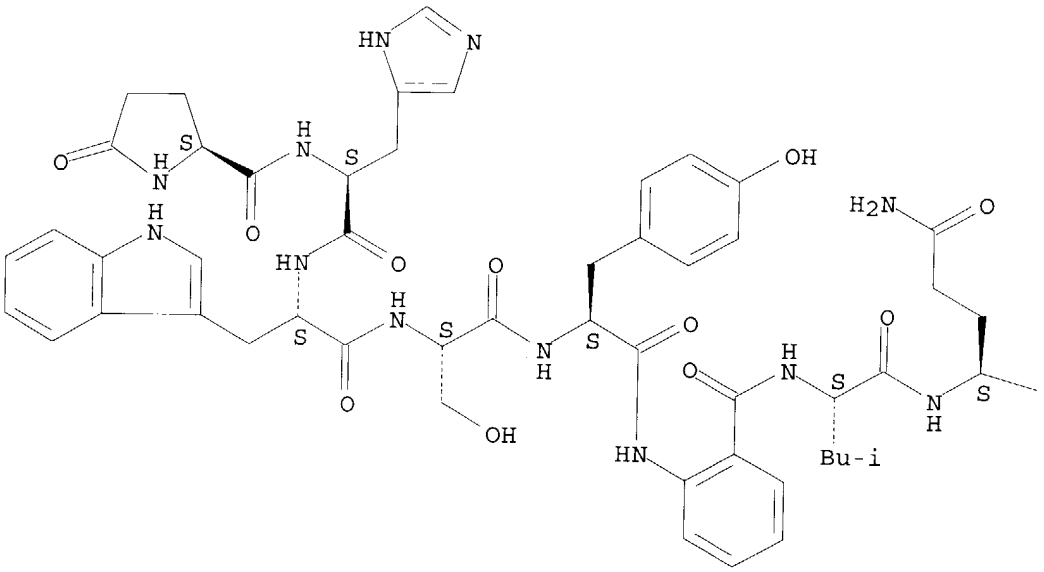
PRIORITY APPLN. INFO.: HU 1986-16 19860103

AB Glp-His-Ser-Tyr-X1-X2-X3-Pro-X4 (I; X1 = o- or m-HNC6H4CO; X2 = Leu, Trp, Phe; X3 = Arg, Leu, Glu; X4 = Gly-NH2, NHEt; Glp = pyroglutamyl) were prepared as LHRH analogs (no data). Glp-His-Trp-Ser-Tyr-Aa-Leu-Gln-Pro-NHEt (Aa = anthranilic acid residue) was prepared using the solution-phase method. Injections containing 1-10 mg I/mL water, saline, or aqueous buffer may be prepared

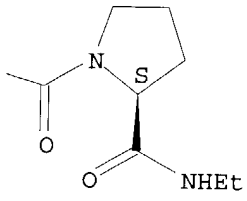
IT **111331-69-2P 111331-70-5P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as **drug**)
RN 111331-69-2 HCAPLUS
CN Luteinizing hormone-releasing factor (swine), 6-(2-aminobenzoic acid)-8-L-glutamine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



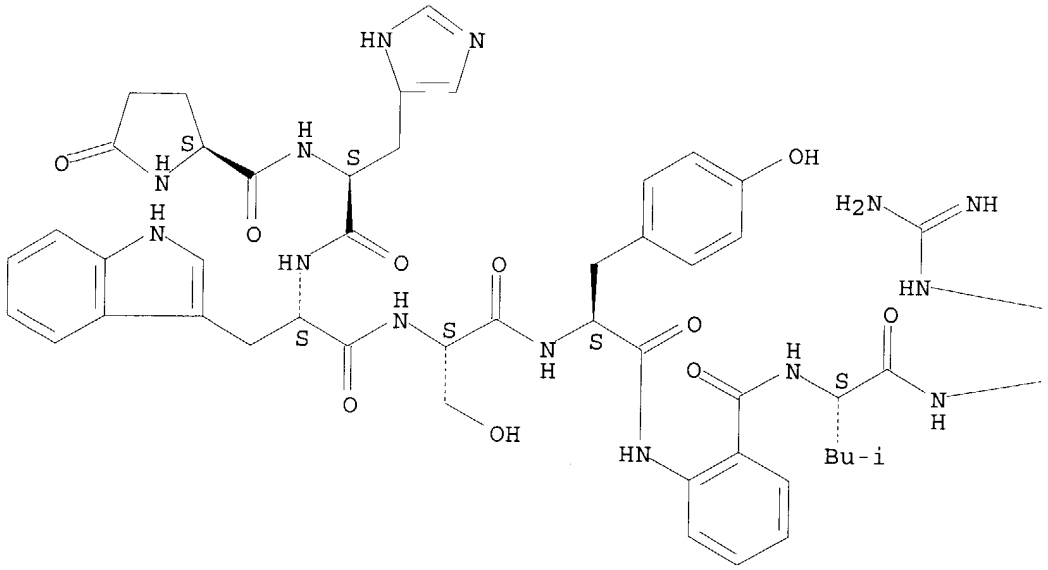
PAGE 1-B



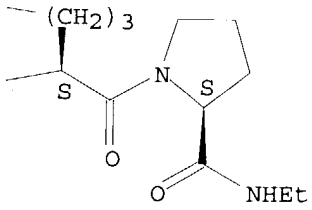
RN 111331-70-5 HCAPLUS
CN Luteinizing hormone-releasing factor (swine), 6-(2-aminobenzoic acid)-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



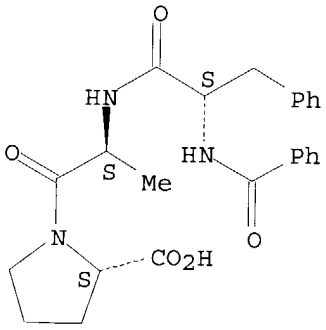
PAGE 1-B



L29 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1986:569766 HCAPLUS
DOCUMENT NUMBER: 105:169766
TITLE: Effects of alveolar pressure on lung angiotensin-converting enzyme function in vivo
AUTHOR(S): Toivonen, Hannu J.; Catravas, John D.
CORPORATE SOURCE: Dep. Pharmacol. Toxicol., Med. Coll. Georgia, Augusta, GA, 30912, USA
SOURCE: Journal of Applied Physiology (1986), 61(3), 1041-50
CODEN: JAPHEV; ISSN: 8750-7587

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of airway pressure on endothelial plasmalemmal angiotensin-converting enzyme function were studied in rabbit lungs in vivo. Static inflation of the lungs to a pressure of 0 or 5 Torr did not change percent transpulmonary metabolism and Amax/Km ratio (defined as enzyme mass (E) + catalytic constant (Kcat)Km and thus, under normal conditions, an indirect measure of perfused endothelial luminal surface area) compared with control measurements during conventional mech. ventilation. When the inflation pressure was increased to 10 Torr, percent metabolism of 3H-labeled benzoyl-L-phenylalanyl-L-alanyl-L-proline (BPAP) remained unaltered but Amax/Km decreased to 60% of the control value. This decrease was in close relation to the decrease in pulmonary blood flow. Addition of 5 cmH2O pos. end-expiratory pressure (PEEP) to the mech. ventilation also decreased Amax/Km values and pulmonary blood flow but did not influence percent metabolism [3H]BPAP. These results suggest that the detected alterations in apparent enzyme kinetics were more likely due to hemodynamic changes than to alterations in angiotensin-converting enzyme function. Thus, high static alveolar pressures as well as PEEP probably reduced the fraction of perfused microvessels as reflected in changes in Amax/Km ratios. This information should prove useful in interpreting the response of pulmonary endothelial enzymes to injury.
IT **69677-91-4**
RL: PRP (Properties)
(degradation of, by angiotensin-converting enzyme of lung, kinetics of, alveolar pressure effect on)
RN 69677-91-4 HCAPLUS
CN L-Proline, N-benzoyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1984:18361 HCAPLUS
DOCUMENT NUMBER: 100:18361
TITLE: Pulmonary metabolic function in the awake lamb: effect of development and hypoxia
AUTHOR(S): Pitt, Bruce R.; Lister, George
CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, 06510, USA
SOURCE: Journal of Applied Physiology: Respiratory, Environmental and Exercise Physiology (1983), 55(2), 383-91
CODEN: JARPDU; ISSN: 0161-7567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of postnatal development and acute alveolar hypoxia on pulmonary metabolic function was studied in conscious newborn lambs. The ability of the lungs of these animals to metabolize 3H-labeled

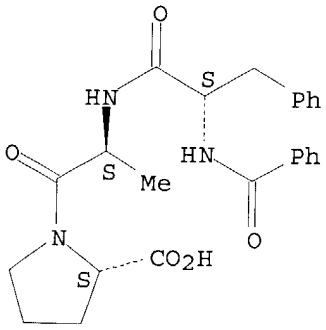
benzoyl-L-phenylalanyl-L-alanyl-L-proline (BPAP) [**69677-91-4**], a synthetic substrate for angiotensin-converting enzyme (ACE) [9015-82-1], and to remove 14C-labeled 5-hydroxytryptamine (5-HT) [50-67-9] were determined during normoxic and hypoxic conditions at 1 day, 1 wk, and 1 mo of age. Addnl. sheep (8-23-wk-old) were studied acutely as adult controls. BPAP metabolism in the 1-day-old group was 48% and increased slowly to 57% at 1 mo of age and to 79% by 23 wk of age. Pulmonary 5-HT removal was adultlike at birth. Alveolar hypoxia significantly decreased BPAP only in the 1-day-old group and had no significant effect on 5-HT removal over the range of ages studied. These data demonstrate a selective and gradual postnatal development of pulmonary ACE which could be due to alterations in either the affinity or maximum capacity of pulmonary ACE, or increased endothelial cell surface area secondary to rapid growth of small blood vessels in this period. Alveolar hypoxia does not appear to closely regulate either ACE activity or 5-HT removal in conscious lambs >1 day old when trace amts. of substrate are used.

IT **69677-91-4**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of, by lung during development, hypoxia effect on)

RN 69677-91-4 HCAPLUS

CN L-Proline, N-benzoyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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